IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	10/789,422
Cnfrm. No.	:	5255
Applicant	:	Boris Y. Shekunov et al.
Filed	:	February 27, 2004
Title	:	METHOD AND APPARATUS FOR PRODUCING PARTICLES USING SUPERCRITICAL FLUID
TC/A.U.	:	1723
Examiner	:	Joseph W. Drodge
Docket No.	:	FER-14668.001

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDED APPEAL BRIEF

Sir:

This Amended Appeal Brief is being filed in response to the Notice of Non-Compliant Appeal Brief mailed on April 30, 2007 (Paper No./Mail Date: 20070427), and clarifies in the "Status of Claims" section that claims 1-16 are pending in the application, and that the final rejection of all such claims is being appealed.

I. REAL PARTY IN INTEREST

The real party in interest or owner of the present application and the technology and inventions embodied therein is Ferro Corporation, whose principal mailing address is 1000 Lakeside Avenue, Cleveland, Ohio 44114. An assignment transferring rights from the inventors to Ferro Corporation was recorded on June 18, 2004 at Reel 015486, Frame 0452.

II. RELATED APPEALS AND INTERFERENCES

The application is not involved in an interference proceeding and there are no related appeals.

III. STATUS OF CLAIMS

The application was filed on February 27, 2004 with sixteen claims. All sixteen claims were rejected in a non-final Office Action mailed on June 15, 2006. Applicants amended all three independent claims, namely claims 1, 11 and 16, in an Amendment filed on September 12, 2006. The Examiner maintained the rejection of all 16 claims in an Office Action mailed on October 24, 2006, and made the rejection thereof final. Thus, claims 1-16 are pending in the application, and the final rejection of all such claims is being appealed.

The pending claims are set forth in the Claims Appendix, which is attached hereto for the convenience of the Board.

IV. STATUS OF AMENDMENTS

No amendments were filed in the application subsequent to the final rejection mailed October 24, 2006.

V. SUMMARY OF CLAIMED SUBJECT MATTER

As described in the application, the present invention provides a method of producing particles using a supercritical fluid. In accordance with the method, a first solvent that is soluble in the supercritical fluid, a second solvent that is substantially insoluble in the supercritical fluid and is at least partially soluble in or miscible with the first solvent, and a solute that is soluble in the first solvent and is substantially insoluble in the second solvent and in the supercritical fluid are contacted together to form a solution. The solution is contacted with the supercritical fluid, which rapidly extracts the first solvent from the solution causing the solute previously solubilized by the first solvent to precipitate in the form of particles that become suspended in the second solvent. The supercritical fluid, which is maintained in a supercritical state throughout the process, carries the first solvent away as it flows through the reactor, thereby separating the particles suspended in the second solvent from the first solvent dissolved in the supercritical fluid. Once the suspension of solute particles in the second solvent has been separated from the first solvent, the suspension of solute particles is separated from the supercritical fluid, either through a drain or by depressurizing a batch processing reactor.

In an effort to fully comply with the requirements set forth in 37 C.F.R. §41.37(c)(1)(v), independent claims 1, 11 and 16 are repeated verbatim below with references to the specification by page and line number added parenthetically:

Claim 1: A method of producing particles comprising:

providing:

a supercritical fluid;

a first solvent that is soluble in the supercritical fluid;

a second solvent that is substantially insoluble in the supercritical fluid and is at least partially soluble in or miscible with the first solvent; and

a solute that is soluble in the first solvent and is substantially insoluble in the second solvent and the supercritical fluid (see page 2, lines 5-10);

contacting the first solvent, the second solvent and the solute together to form a solution (see page 2, lines 6-10);

contacting the solution with the supercritical fluid to extract the first solvent from the solution and precipitate the solute in the form of particles that are suspended in the second solvent (see page 2, lines 10-13); and

separating the particles suspended in the second solvent from the first solvent dissolved in the supercritical fluid when the supercritical fluid is in a supercritical state (see page 7, lines 10-16).

Claim 11: A method of producing particles comprising:

providing:

supercritical carbon dioxide (see page 3, lines 1-2);

an organic solvent that is substantially soluble in supercritical carbon dioxide (see page 3, line 11);

water (see page 3, line 15); and

a biologically active substance that is soluble in the organic solvent and is substantially insoluble in water and supercritical carbon dioxide (see page 3, lines 17-20);

contacting the organic solvent, water and biologically active substance together to form a solution (see page 3, lines 23-24);

contacting the solution with the supercritical carbon dioxide to extract the

organic solvent from the solution and precipitate the biologically active substance in the form of particles that are suspended in water (see page 4, lines 3-5); and

separating the particles suspended in water from the organic solvent dissolved in the supercritical carbon dioxide when the supercritical carbon dioxide is in a supercritical state (see page 7, lines 10-16).

Claim 16: An apparatus for producing particles comprising:

an extraction vessel (see page 4, lines 22-23);

a first reservoir for holding a supply of supercritical fluid ;

a first pump for pumping supercritical fluid from the first reservoir to the extraction vessel (see page 4, line 31 to page 5, line 1; and original claim 16 - see: *In re Gardner*, 480 F.2d 879; 178 U.S.P.Q. 149 (C.C.P.A. 1973));

a second reservoir for holding a supply of solution, the solution comprising:

a first solvent that is soluble in the supercritical fluid;

a second solvent that is substantially insoluble in the supercritical fluid and is at least partially soluble in or miscible with the first solvent; and

a solute that is soluble in the first solvent and is substantially insoluble in the second solvent and the supercritical fluid;

a second pump for pumping solution from the second reservoir to the extraction vessel (see page 5, lines 1-2; and original claim 16 - see: *In re Gardner*, 480 F.2d 879; 178 U.S.P.Q. 149 (C.C.P.A. 1973));

a release valve for removing a mixture comprising the first solvent dissolved in the supercritical fluid from the extraction vessel when the supercritical fluid is in a supercritical state to separate the first solvent from particles of the solute suspended in the second solvent (see page 5, lines 2-3; and page 7, lines 15-17); and

means for removing particles of the solute suspended in the second solvent from the extraction vessel (see page 7, lines 19-30).

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Whether claims 1-16 were properly rejected under 35 U.S.C. §102b) as anticipated by Sievers et al., U.S. 5,639,441.

VII. ARGUMENT

The Examiner rejected claims 1-16 under 35 U.S.C. §102(b) as being anticipated by Sievers et al., U.S. Pat. 5,639,441. For the reasons set forth below, applicants respectfully submit that the Examiner's rejection of such claims was improper, and should be reversed.

A. Claims 1-10 (Grouped) Were Improperly Rejected Under 35 U.S.C. §102(b)

The prior art reference relied upon by the Examiner to reject claims 1-10, namely Sievers et al., discloses a method for forming a gas-borne dispersion of fine particles of a desired substance that involves: (a) substantially dissolving or suspending the desired substance in a first nongaseous fluid to form a first solution or suspension; (b) mixing the first solution or suspension with a second nongaseous fluid to form a composition comprising the substance and an immiscible mixture of the first and second nongaseous fluids; and (c) rapidly reducing the pressure on the composition whereby at least one of the nongaseous fluids forms a gas, and whereby a gas-borne dispersion of fine particles of the substance is formed (see col. 4, line 61 to col. 5, line 7). The Examiner contends that Sievers et al. anticipates applicants' invention as claimed in claim 1. Applicants respectfully disagree.

As noted above, claim 1 requires the provision of at least the following:

(I) a supercritical fluid;

(II) a first solvent that is soluble in the supercritical fluid;

(III) a second solvent that is substantially insoluble in the supercritical fluid and is at least partially soluble in or miscible with the first solvent; and

(IV) a solute that is soluble in the first solvent and is substantially insoluble in the second solvent and the supercritical fluid.

Claim 1 of the present invention further requires that the first solvent (II), the second solvent (III) and the solute (IV) be contacted together to form a solution (II + III + IV). Claim 1 further requires that the solution (II + III + IV) be contacted with the supercritical fluid (I), which

extracts the first solvent (II) from the solution (II + III + IV) thereby causing the solute (IV) to precipitate in the form of particles that become suspended in the second solvent (III + IV). Lastly, claim 1 of the present invention requires that the solute particles suspended in the second solvent (III + IV) be separated from the first solvent that is dissolved in the supercritical fluid (I + II) when the supercritical fluid (I) is in a supercritical state. Sievers et al. clearly does not disclose, teach or suggest such a process.

The Examiner contends that since Sievers et al. states that both the first fluid and the second fluid could be supercritical fluids (see col. 6, lines 49-52), and because Sievers teaches that only one of the first fluid or the second fluid needs to pass into a gaseous state (see col. 6, lines 17-2), Sievers et al. anticipates applicants' invention because one of the supercritical fluids could remain in a supercritical state when particle formation occurs. But this reasoning is flawed.

If, as argued by the Examiner, one of skill in the art was motivated by Sievers et al. to mix a desired substance with two immiscible supercritical fluids to form a composition, and then rapidly reduce the pressure on the composition such that one of the two supercritical fluids became gaseous and formed a gas-borne dispersion of the desired substance suspended in the other supercritical fluid which remained in a supercritical state, such process would not read on applicants' method as claimed in claim 1. The result produced by such a method would be a gas-borne dispersion of the desired substance suspended in the still supercritical fluid, but such a process would not include a step of separating a solvent that is soluble in the supercritical fluid from the particle suspension while the supercritical fluid that extracted the solvent was in a supercritical state.

This can be explained with greater clarity using the same symbols as used above to describe the essential four components of applicants' method as claimed in claim 1. If Sievers et al. is read as argued by the Examiner, one would form a composition comprising an immiscible mixture of a first supercritical fluid (I), a second supercritical fluid (III) and a desired substance (IV). The second supercritical fluid (III) in the Examiner's proposed process according to Sievers et al. would have to correspond to applicants' second solvent (III) inasmuch as applicants' second solvent (III) and the second supercritical fluid (III) according to the process according to Sievers et al. must be immiscible with the first supercritical fluid (I). In order to include a first solvent (II) in the composition according to Sievers et al., one of skill in the art would have had to be motivated to include an additional solvent in the composition. Applicants note that Sievers et al. does state that the first and second fluids may contain co-

solvents and antisolvents (see col. 6, lines 53-54). However, even if one were motivated to include a co-solvent or antisolvent that could correspond to applicants' first solvent (II), Sievers et al. would not read on applicants' method as claimed in claim 1 because Sievers et al. does not teach that such co-solvent or antisolvent should be separated from a suspension of the desired substance in the second supercritical fluid (III + IV) while the first supercritical fluid (I) is in a supercritical state. No matter how far the teachings of Sievers et al. are stretched beyond their intended scope by the Examiner, Sievers et al. simply cannot be fairly read to anticipate the method as claimed in claim 1. The rejection of claims 1-10 under 35 U.S.C. §102(b) is improper and should be reversed.

B. Claims 11-15 (Grouped) Were Improperly Rejected Under 35 U.S.C. §102(b)

Claim 11 includes the same process steps as claimed in claim 1, but is more specific regarding the four essential components of the method. Specifically, claim 11 requires the provision of at least the following:

(I) supercritical carbon dioxide;

(II) an organic solvent that is substantially soluble in supercritical carbon dioxide;

(II) water; and

(IV) a biologically active substance that is soluble in the organic solvent and is substantially insoluble in water and supercritical carbon dioxide.

Sievers et al. states that in one preferred embodiment of the invention, the first fluid (III) comprises water and the second fluid is supercritical carbon dioxide (I) (see col. 6, lines 57-61). However, contrary to applicants' claimed method, Sievers et al. also teaches that the desired substance (IV) is dissolved in water (see col. 6, lines 57-61). However, inasmuch as Sievers et al. indicates that mixtures of components such as methanol and water (see col. 6, line 56) can be used, one could conceive of a mixture that included a desired substance that was soluble in

methanol, but insoluble in water. Methanol is an organic solvent (II) that is soluble in supercritical carbon dioxide.

Thus, following the disclosure of Sievers et al., one could arrive at the four essential components that must be provided in accordance with applicants' method as claimed in claim 11. However, Sievers et al. does not fairly teach extracting the methanol into the supercritical carbon dioxide to precipitate particles of the desired substance such that they become suspended in the water, and further does not fairly teach separating the methanol from the aqueous suspension of the desired substance while the supercritical fluid is in a supercritical state. If one followed the process according to Sievers et al., one would simply rapidly release the pressure on the mixture of supercritical fluid, water, methanol and desired substance to cause the supercritical fluid to explosively form a gas, which thereby formed a gas-borne dispersion of the desired substance, methanol and water. There simply is no way to read Sievers et al. on claim 11.

C. Claim 16 Was Improperly Rejected Under 35 U.S.C. §102(b)

Claim 16 claims the apparatus for practicing the method as claimed in claim 1. The Examiner contends that the apparatus as claimed in claim 16 is anticipated by the apparatus disclosed in Sievers et al. Applicants respectfully disagree.

Apparatus for carrying out the process according to Sievers et al. is depicted in Figs. 1 and 2 and described from col. 11, line 44 through col. 13, line 11. In the embodiment depicted in Fig. 1, the apparatus includes a pump (12) for pumping a supercritical fluid from a reservoir (10) to a mixing tee (20). An aqueous solution containing the desired substance is also pumped from a reservoir (14) using a pump (16) to the mixing tee (20). The supercritical fluid and aqueous solution mix together in the mixing tee (20) and pass through a small diameter capillary restrictor (22) whereupon the supercritical fluid rapidly expands due to a decrease in pressure forming a gas-borne dispersion of the aqueous solution of the desired substance. In the embodiment depicted in Fig. 2, a composition comprising an immiscible mixture of supercritical fluid and an aqueous solution of the desired substance is retained in a canister (46) that is provided with a cap (54). Rotation of the cap (54) causes a puncturing pin (50) to puncture a septum (48), allowing the composition to pass through an orifice (52). The supercritical fluid in the composition rapidly expands to form a gas upon exiting the canister (46), thereby forming a gas-borne dispersion of the aqueous solution and desired substance (56).

The Examiner contends that the apparatus according to Sievers et al. anticipates the apparatus as claimed in claim 16. Applicants respectfully disagree. Claim 16 claims (bold, italicized and underlined emphasis added):

> An apparatus for producing particles comprising:
> an extraction vessel;
> a first reservoir for holding a supply of supercritical fluid ;
> a first pump for pumping supercritical fluid from the first reservoir to the extraction vessel;
> a second reservoir for holding a supply of solution, the solution comprising:
> a first solvent that is soluble in the supercritical fluid;
> a second solvent that is substantially insoluble in the supercritical fluid and is at least partially soluble in or miscible with the first solvent; and
> a solute that is soluble in the first solvent and is substantially insoluble in the second solvent and the supercritical fluid;
> a second pump for pumping solution from the second reservoir to the extraction vessel;
> ***a release valve for removing a mixture comprising the first solvent dissolved in the supercritical fluid from the extraction vessel when the supercritical fluid is in a supercritical state <u>to separate the first solvent from particles of the solute suspended in the second solvent</u>;*** and
> means for removing particles of the solute suspended in the second solvent from the extraction vessel.

Neither embodiment of an apparatus according to Sievers et al. includes a release valve in communication with an extraction vessel that separates a first solvent from particles of solute suspended in a second solvent. The apparatus according to Sievers et al. has one opening which allows the entire mixture of components to escape to a region of lower pressure. Accordingly, the rejection of claim 16 is clearly improper.

Conclusion

In view of the foregoing, it is respectfully submitted that claims 1-16 are allowable over the prior art references of record, and a ruling from the Board to that effect is therefore respectfully requested.

Respectfully submitted,

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CLAIMS APPENDIX

Claim 1 (previously presented): A method of producing particles comprising:

providing:

a supercritical fluid;

a first solvent that is soluble in the supercritical fluid;

a second solvent that is substantially insoluble in the supercritical fluid and is at least partially soluble in or miscible with the first solvent; and

a solute that is soluble in the first solvent and is substantially insoluble in the second solvent and the supercritical fluid;

contacting the first solvent, the second solvent and the solute together to form a solution;

contacting the solution with the supercritical fluid to extract the first solvent from the solution and precipitate the solute in the form of particles that are suspended in the second solvent; and

separating the particles suspended in the second solvent from the first solvent dissolved in the supercritical fluid when the supercritical fluid is in a supercritical state.

Claim 2 (original): The method according to claim 1 wherein the solute comprises a biologically active substance.

Claim 3 (original): The method according to claim 1 wherein the supercritical fluid is selected from the group consisting of supercritical carbon dioxide, dimethylether, straight chain or branched chain C1-C6 alkanes and combinations thereof.

Claim 4 (original): The method according to claim 1 wherein the solution further comprises a plurality of solutes and wherein the particles suspended in the second solvent comprise the plurality of solutes.

Claim 5 (original): The method according to claim 4 wherein the plurality of solutes comprises a first solute comprising a biologically active substance and a second solute comprising an excipient selected from the group consisting of a polymer, a wax, a lipid and combinations thereof.

Claim 6 (original): The method according to claim 1 wherein the first solvent comprises an organic solvent.

Claim 7 (original): The method according to claim 6 wherein the first solvent is selected from the group consisting of dimethyl formamide, dimethyl sulfoxide, alcohols, acetone, ethyl acetate and chloroform.

Claim 8 (original): The method according to claim 1 wherein the second solvent is water.

Claim 9 (original): The method according to claim 1 wherein the average particle size of the particles suspended in the second solvent is from about 10 nm to about 10 μm.

Claim 10 (original): Particles formed according to the method of claim 1.

Claim 11 (previously presented): A method of producing particles comprising:

providing:

supercritical carbon dioxide;

an organic solvent that is substantially soluble in supercritical carbon dioxide;

water; and

a biologically active substance that is soluble in the organic solvent and is substantially insoluble in water and supercritical carbon dioxide;

contacting the organic solvent, water and biologically active substance together to form a solution;

contacting the solution with the supercritical carbon dioxide to extract the organic solvent from the solution and precipitate the biologically active substance in the form of particles that are suspended in water; and

separating the particles suspended in water from the organic solvent dissolved in the supercritical carbon dioxide when the supercritical carbon dioxide is in a supercritical state.

Claim 12 (original): The method according to claim 11 wherein the solution further comprises a second solute comprising an excipient selected from the group consisting of

polymers, waxes, lipids and combinations thereof, and the particles suspended in water comprise the biologically active substance and the excipient.

Claim 13 (original): The method according to claim 11 wherein the organic solvent is selected from the group consisting of dimethyl formamide, dimethyl sulfoxide, alcohols, acetone, ethyl acetate and chloroform.

Claim 14 (original): The method according to claim 11 wherein the average particle size of the particles suspended in water is from about 10 nm to about 10 μm.

Claim 15 (original): Particles formed according to the method of claim 11.

Claim 16 (previously presented): An apparatus for producing particles comprising:
an extraction vessel;
a first reservoir for holding a supply of supercritical fluid;
a first pump for pumping supercritical fluid from the first reservoir to the extraction vessel;
a second reservoir for holding a supply of solution, the solution comprising:
a first solvent that is soluble in the supercritical fluid;
a second solvent that is substantially insoluble in the supercritical fluid and is at least partially soluble in or miscible with the first solvent; and
a solute that is soluble in the first solvent and is substantially insoluble in the second solvent and the supercritical fluid;
a second pump for pumping solution from the second reservoir to the extraction vessel;
a release valve for removing a mixture comprising the first solvent dissolved in the supercritical fluid from the extraction vessel when the supercritical fluid is in a supercritical state to separate the first solvent from particles of the solute suspended in the second solvent; and
means for removing particles of the solute suspended in the second solvent from the extraction vessel.

EVIDENCE APPENDIX

No evidence was submitted by the applicants pursuant to 37 C.F.R. §1.130, 1.131 or 1.132, and no evidence was entered by the Examiner and relied upon by the applicants in this appeal.

RELATED PROCEEDINGS APPENDIX

There are no related proceedings.